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The University of Toronto Medical Journal

VOL. I FEBRUARY, 1924 NO. 3

EDITORIAL

THE JOURNAL continues to be well received, a fact which gives the Editors and the Medical Society the deepest satisfaction. When we have seen the next two issues in the hands of our readers, we will know whether or not the enterprise is justified. The members of the faculty, junior and senior, have been splendid in their support of the publication and to them we extend our heartiest thanks and hope for the same co-operation in the future. We have received encouraging comment from numerous outside quarters and reprint with pleasure in this issue, an excerpt from a letter received from our sister University, Queen's.

We are fortunate in having as an adviser, Dr. Norman B. Gwyn, of the staff in Medicine. Dr. Gwyn has kindly consented to help us through our many difficulties and we feel that with such a man assisting us, our position is greatly consolidated. Through his efforts we hope to be reviewed by the Canadian and American Medical Association Journals and, in addition, an exchange department is a distinct prospect.

SOME interesting work is going on in the Burnside Obstetrical Department of the General Hospital at the instigation of Dr. W. G. Cosbie of the Obstetrical staff. Dr. Cosbie became interested in a report from New York on rectal anaesthesia in labour and saw its possibilities. At his suggestion, Dr. W. A. Dafoe, the resident at the Burnside, has launched a vigorous and thorough investigation of the efficiency of anaesthesia introduced per rectum following the onset of labour. Ether in glycerin, combined with a hypodermic injection of morphine and magnesium sulphate, is the combination that is being tried out and gratifying results have been already achieved by the investigator. Dr. Dafoe is using rectal anaesthesia on all primiparas and will report on a series of cases when he has it complete. If a satisfactory technique can be worked out the procedure will be of inestimable value in easing the pain of labour. Dr. Dafoe's report will be awaited with interest.

DR. W. E. GALLIE has been honoured very highly by the Royal College of Surgeons, of which he is a Fellow, by being appointed a Hunterian Professor for 1924. No Fellow in Canada has had this honour conferred on him in the last twenty years. We feel glad that this recognition has come to one of our distinguished professors and on behalf of the whole student body congratulate Dr. Gallie.

The Hunterian Professorship was established about 110 years ago as one of the conditions on which the Hunterian Collection was transferred to the College of Surgeons.

The practice at the present time is to have a selected group of eminent Fellows of the College each deliver one or more lectures on subjects which they have advanced by original research, the total number of lectures delivered being not less than twelve.

Among the famous men who have been Hunterian Professors in the past are the following: Sir Benjamin Collins Brodie, Richard Owen, Sir Frederick Treves, Lord Lister, Ernest Wm. Hey Groves, Louis Bath Rawling, Sir Berkeley Moynihan and William Sampson-Handley.

Dr. Gallie graduated from the University of Toronto in 1903. He was on the surgical staff of the Toronto General Hospital from 1908 to 1912, and since that time has been Surgeon-in-Chief to the Hospital for Sick Children. He has taken an active part in original investigations, his chief contributions having been in connection with the healing of bones and the effects of transplants of bone and fascia. The subject-matter for his lecture before the Royal College of Surgeons is the results he has attained in the latter line of investigation, or more definitely, the use of living sutures of fascia in the repair of anatomical defects.

Dr. Gallie was not satisfied with the results obtained by the current operations for the cure of ventral hernias and other conditions where the results depend on the strength of scar tissue. Hence he commenced an investigation into the process of union of sutured fascia. During the course of his investigations the idea occurred to him of using strips of fascia as sutures actually to sew the separated structures together. He found this process to attain the very ends for which he had been striving, and not only could he sew structures together but he could block effectively by a sort of darning, spaces between structures which could not be pulled into apposition. The sutures being living matter are absolutely non-irritating. They continue to live in their new situation without stretching or losing any strength.

Using fascia lata, this method has been employed clinically in a great many cases, and some years have been allowed to elapse to apply the test of time. The results have been uniformly successful and Dr. Gallie now feels perfectly confident that the method will solve the problem of the repair of difficult hernias and other anatomical defects. Dr. A. B. LeMesurier has been associated with Dr. Gallie in this work.

Our wish for Dr. Gallie is a warm reception and a very pleasant holiday.

THE recently published Transactions of the American Association for Thoracic Surgery give a prominent place to a discussion of the problems of pneumothorax and intra-pleural tension. A great deal of confusion occurs in the literature on this subject, but in the main two views are held—the one that the pleural cavities are to be considered as an anatomic unity, and the opposed view that they are essentially a duality. The trouble seems to be that there is conflicting experimental evidence on the whole question. Its solution has a direct bearing on the question of the open operation for empyema, of therapeutic induction of pneumothorax in tuberculosis, and in the many problems of thoracic surgery.

It will be remembered that in 1918 in the American army as a result of the epidemic of influenza with a high incidence of following empyema a new interest was given to the study of the mechanics involved in pneu-

mothorax, there being a high mortality from pneumothorax caused by early operation in these cases of acute empyema. At that time Graham and Bell conducted a series of experimental investigations on animals and human cadavers to throw some light on the whole question of the open operation for drainage of an empyema. They found that any alteration in pressure in the one pleural cavity is accompanied by an alteration in pressure in the other to the same extent, that the size of the opening is of importance, that the vital capacity of the individual is a prime factor, and that the presence of adhesions or of thicknening of the mediastinal structures materially change the effects of an alteration of pressure in the one pleural cavity. As a result they advised delaying operation in drainage of an empyema until adhesions had formed. The application of these findings undoubtedly saved many lives in the subsequent handling of post-influenza empyema.

Since then their conclusions have been very severely criticized, notably by M. Duval, who contends that Graham's conclusions based upon experiments on dogs are fallacious, because in the dog the pleural cavities intercommunicate and therefore that a one-sided thoracotomy leads to a bilateral pneumothorax with fatal collapse of both lungs. This does not hold in man. War surgery on the chest tended to support Duval's contention that a one-sided pneumothorax is limited to the side operated on.

At the meeting of the Association for Thoracic Surgery, Snyder of the Mayo Foundation supports Duval's position. His experiments lead him to the view that conclusions from experiments on the dog are erroneous for the anterior mediastinum in the dog is of the thinness of paper, permeable to air and fluids, while in man it is of some thickness and resistance. Pneumothorax in man, if unilateral in origin remains unilateral and the change of intrapleural tension on the opposite side is compensated for by a deviation of the mediastinum. Snyder also concludes that cohesion is probably not a factor in maintaining the expansion of the lungs.

We still are faced, therefore, with two interpretations based on conflicting experimental results. The conclusion seems to be that in spite of possible doubt thrown on certain of his conclusions, Graham has done a service by emphasizing the danger of an open pneumothorax and that such a procedure is in direct relationship to the vital capacity and relative mobility of the mediastinum. It would seem, however, that this fundamental question in physiology as to what happens when the chest is opened is still unsettled.

WE wish to acknowledge the support which we have received from undergraduate members of Queen's University in the form of a substantial number of subscriptions to the *Medical Journal* for the balance of the year. We are in receipt of the following from the Editor of the Queen's University Journal: "The articles in your journal certainly fill a long-felt need in that they are written with an eye to the student's education rather than mystification. This has been the serious fault to be found with so many of the graduate papers—only occasionally is one able to pick out an article suited to his necessarily limited knowledge, both theoretical and practical."

In Memoriam

Charles Kirk Clarke, M.D., LL.D., Professor of Psychiatry in the University of Toronto, and late Dean of the Faculty of Medicine, son of Hon. Lt. Col. Charles Clarke and Emma (Kent) Clarke, was born at Elora, Ont., February 16th, 1857. He graduated from the University of Toronto with the degree of M.B. in 1878 and received the degree of M.D. in the following year. He began his medical career under the tutelage of Joseph Workman, M.D. He was a clinical assistant at the Toronto Hospital for Insane from 1874 to 1878; assistant physician at the same institution from 1878 to 1879; assistant superintendent of Hamilton Hospital for Insane 1879 to 1881; assistant superintendent, then superintendent of Rockwood Hospital for Insane, Kingston, from 1881 to 1905. During this latter period he was Professor of Psychiarty in Queen's University and received the honorary degree of LL.D. from that university in 1906. He came to Toronto in 1905 and served as superintendent of Toronto Hospital for Insane till 1911, and held the position of Medical Superintendent, Toronto General Hospital, 1911-1918. Since 1918, he has been Medical Director of the Canadian National Committee for Mental Hygiene. He became Professor of Psychiatry at the University of Toronto in 1907 and was Dean of the Medical Faculty in this University from 1908 to 1920.

Dr. Clarke had the rare privilege of seeing many of the dreams of his early life come true in his later years. He was a prime believer in humanitarian ideals in the treatment of the insane, and he lived to see the principle of non-restraint established in mental hospitals throughout the Dominion. At the outset of his career a psychiatrist was a custodian of insane patients while now psychiatry is a science, mental diseases being diagnosed, and classified, and treated accordingly.

The climax of his long and active career was reached during the closing year of his life. In May, 1923, he delivered the Maudsley lecture in Psychiatry at the Congress of the British Medico-Psychological Association in London, England. Last fall he laid the corner stone of the new Reception Hospital for Mental Patients in connection with the Toronto General Hospital. Since his investigation of the methods and treatment of mental diseases in Europe in 1907, he has advocated the building of such a hospital, and it is largely due to his efforts that this institution has at last been established.

Dr. Clarke was not only an expert alienist but also an educational reformer, a naturalist, a musical amateur, a versifier, an authority on Canadian literature, and an apostle of the outdoor. A man of many sided activities, the thing that lay closest to his heart was his regard for the interests of the medical students of this University.

THE TREATMENT OF COMPOUND FRACTURES OF LONG BONES*

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In these modern days when so many advances are being made in scientific medicine and surgery it seems almost necessary to apologize for the presentation of a paper on so ancient and commonplace a subject as the treatment of compound fractures. The fact remains, however, that anyone who sees and studies the end results of a large series of these cases from a standpoint of function, finds much to be desired. The further fact, that a multitude of methods are advocated by as many surgeons and teachers, shows that the last word has not been written on this subject. The problem is worth considering because it has been shown that the victims of such accidents are always very severely disabled, and are prevented for many months and often years from returning to any form of occupation, and when returned may be efficient only to a very small percentage of their previous ability. This results yearly in a very large industrial and economic loss. It is the duty of the surgeon to assist in every possible way the very worthy efforts that are being put forward by industrial concerns and other agencies to lessen the period of disability in these and similar accidents, and to increase the ultimate efficiency of the individual so afflicted.

In an attempt to arrive at a reason why fractures in general, and severe compound fractures in particular, are so badly handled by the bulk of practitioners one is faced with several possibilities:

1. The usual text-book teaching of care of fractures is necessarily handled briefly, and often the methods advocated are open to criticism. The student is not able to separate the salient facts and the general principles of treatment are lost on him; hence he needs a closer clinical contact with actual cases.

2. The teaching of fracture treatment is difficult, as most of these are emergency cases and the actual handling of such takes place when the students are not in attendance. They see patients only in splints or more or less fixed permanent dressings. This can be remedied by a compulsory interne service for all students, or by post graduate work.

3. The treatment of fractures requires a high degree of mechanical ability not possessed by all practitioners. Industrial concerns are not slow to recognize this fact, and a great many are employing specially trained men to look after all of their industrial accidents. The Compensation Boards of states or provinces are also interested in getting men back to duty in as short a period as possible and with as little loss of function as possible, and they are advocating special training for surgeons undertaking such treatment. The final advance would be the appointment of a specially qualified surgeon, devoting his entire time to the duty, to act as a travelling consultant for a certain district to see all serious accident cases and advise as to their care.

*Delivered at Tri-State District Medical Association, Des Moines, Nov. 1, 1923.

For the purpose of this paper the compound fractures are best divided into two classes:—

1. Those compounded from within; the wound usually is small and made by a spicule of bone which has penetrated the skin.

2. Those compounded from without, the wound being made by some crushing or penetrating force which is carried to the bone.

In the first class, after the bones are fractured, the force continuing causes the bone end to protrude through the soft structures and penetrate the skin. In most of the cases the act of straightening the limb causes the bone to recede. In only a small percentage of cases does the bone impale the clothing and carry bits of foreign matter into the wound. In the great majority of these cases no sepsis occurs if properly treated by the surgeon who first sees the case, and it may therefore be treated as a simple fracture. The responsibility for the outcome in this type rests almost entirely with the surgeon who does the first dressing. More than ninety per cent. of these cases seen in the emergency and outpatients' departments get well without sepsis.

After removal of clothing the wound should be covered by a small pad of sterile gauze just sufficiently large to cover the wound, and held tightly in place. The skin surface may be cleansed with gasoline from the wound outward to a distance of twelve to fourteen inches, and the limb dry shaved outward from the wound to the same extent. After the gasoline has dried tincture of iodine may be painted on to cover the above area. In children it is always well to rub off iodine subsequently with alcohol to prevent blistering. This area is then covered with sterile towels, the wound itself is cleansed with gasoline, and iodine applied. With a dry dressing and no drainage most of these cases heal kindly by first intention and may be splinted and treated as simple fractures.

In civilian cases where the patient can be brought directly to hospital or surgeon, the application of first aid dressing to the wound by policemen or others is not to be advocated on account of the danger of sepsis.

In the second group of cases the fractures are the result of crushing injuries by heavy machinery or railway accidents, and those comparatively rare civilian cases due to gun shot injuries. In these the destruction of soft tissues is more or less severe, and in some the injury to the vascular structures is so great as to demand immediate amputation. Where the vessels of the limb have escaped most cases are amenable to treatment and secondary amputations for severe sepsis are very rarely necessary.

There are not a few surgeons, who, anxious that the lessons of the war should not be forgotten, advocate very strongly the war methods of dealing with these severe injuries—forgetting that most of the conditions which have to be accepted in war work do not or should not exist in civilian injuries. The injuries in the early years of the war resulted in severe sepsis in practically all cases, and even in the later stages only about three per cent. or less escaped. The first aid dressing was of no avail in preventing sepsis, as the application of iodine on the surface and the application of a sterile dressing could not be expected to be of any value, when it is remembered that the infective material was carried by the ragged missile into the soft tissues of the extremity with the dirty clothing. Many of these cases lay out in "No Man's Land" or were sent down the line, and frequently twenty-four to seventy-two hours elapsed before adequate

surgical aid was available. The common infection in all of these cases was the gas bacillus (bacillus aerogenes capsulatus), and the loss of time made the prognosis exceedingly grave. Tetanus infection was also a common complication in the early stages. The gas bacillus and tetanus infections were undoubtedly due to the fact that all clothing was saturated with the soil of these heavily manured regions. The immediate injection of antitetanic serum by the ambulance medical officer, the sending of surgical teams to the dressing station for early surgical attention, and the improved splinting of these unfortunate cases certainly were large factors in reducing mortality and in saving many limbs and lives. The surgical measures adopted by these advanced teams were radical and effective. They consisted of extensive débridement, removing all non-viable soft tissue, leaving a great open cavity for irrigation and adequate drainage.

It is quite obvious that most of the conditions which existed in the war and which were responsible for the great calamities of war surgery do not and cannot exist in civilian injuries, and consequently much of the necessary surgery of the war would not only be unnecessary in civilian practice, but in many cases would be reprehensible. The industrial injuries happen for the most part to workmen whose skin is clean, the clothing if soiled is not loaded with infective material, and rarely is the clothing carried in and buried in the soft tissues. Except in those injuries in farming communities due to farm machinery we find gas bacillus infection very rarely. In all cases surgical attention is available within an hour or two of the injury, so that the advocates of war methods must largely modify their methods or much harm may result.

In all injuries of this class occurring in railway accidents, in building operations, and even possibly in all cases, a preventive inoculation with antitetanic serum is advisable. In the treatment of the civilian cases in a general way one would say that the first duty is to combat shock. Rest is secured by the administration of a hypodermic injection of morphine. Heat is applied externally by means of hot water bags and blankets. Stimulants in the form of hot coffee may be given, and fluids supplied by interstitial salines and the Murphy drip with glucose.

As soon as safe an anaesthetic should be administered, and the limb carefully examined. The protection of the wound by sterile gauze and the thorough cleansing and shaving of the skin should be done as noted in the first class of cases. The wound should then be dealt with, first the clipping away of all tags of skin, then the removal of all fascia and muscle tissue which is ragged and obviously damaged so extensively that its recovery is unlikely. The muscle tissue which has lost its color and does not bleed or contract on section likely will never be viable, and should be removed. All gross dirt and foreign matter of any sort should be carefully removed. Loose or comminuted fragments of bone should not be removed unless they are practically extruded from the wound and completely separated from all source of blood supply. The extensive removal of these loose fragments is a very frequent source of ultimate non-union. Even fragments which have a doubtful blood supply should be left, as some may recover and the others may easily be removed subsequently if they are found non-viable.

No attempt at primary suture should be made, but the wound left wide open for adequate drainage. Drains of rubber tubes as in the

Carrel Dakin technique may be inserted, or rubber protective and loose gauze may be used and the whole wound irrigated with Dakin's solution every three hours in the daytime, with longer intervals to insure rest at night. If properly splinted with splints of the Thomas pattern to secure good alignment, extension, and support, the wound and the patient should do well. After two weeks of adequate drainage and irrigation, secondary suture may be possible in a fair number of cases. The after-treatment of these cases requires unremitting care to see that drainage is free, irrigation is efficient, and extension is always adequate.

Drainage—Whenever possible wounds should be enlarged to take advantage of gravity drainage. Where this is impossible pockets of discharge should be prevented by constant irrigation or the use of the Taylor suction tank drainage. The use of Bipp—bismuth, iodoform, and petrolatum or paraffin—as advocated by Sir Rutherford Morrison, may be of definite value if properly applied. In the writer's opinion its greatest value is due to the paraffin oil or petrolatum. When it is smeared into a wound thoroughly, leaving only a thin coating on the exposed tissues, it thereby prevents adhesion of the surfaces for a period of forty-eight hours or more, and makes a very efficient form of drainage by preventing the retention of secretions and toxins in the deeper tissues. The gross application of Bipp as so often used to fill the whole cavity defeats the very object for which it was devised, and no wound will heal until this is all removed or discharged.

Splints.—Adequate splinting of a compound fracture at the very earliest moment after injury is an essential feature of treatment. It tends to lessen shock, prevents further injury to soft structures, tends to limit the extension of sepsis and brings comfort and freedom from pain to the patient. In the war it was one of the great factors in lessening the dreadful mortality rate and in improving the chances for ultimate reasonable function. The objects aimed at in successful splinting are:

1. To secure in as great a degree as possible proper alignment of the fractured bones.

2. To recover as nearly as possible the original length of the limb. This is especially necessary in the case of the lower extremity.

3. To immobilize more or less completely the joints above and below the fracture.

4. To afford easy access to the wounds for dressing and irrigation without losing any of the features noted above. The only method of holding a fractured limb which permits of these aims being carried out effectively, is that of extension, and any splint which may be advocated must depend on the principle of extension for its efficiency.

The great lesson of the war so far as fractures are concerned was that which showed the marvellous utility of the Thomas splint in meeting all of the demands as noted above. That the lesson was well learned is amply demonstrated by the fact that in fracture clinics the world over the Thomas splint with many modifications is the chief reliance of the surgeons of such clinics. To Sir Robert Jones is due the real credit for the introduction of this splint, thus supplanting the many antiquated and inefficient splints previously used.

For transport, in fractures of the lower extremity, the usual type of Thomas splint provides the possibility of adequate extension, giving align-

ment and approximate length, with fixation of joints, support of the soft tissues, and easy accessibility for dressing. In hospital the additional suspension from a Balkan frame and extension from the end of the splint will complete the comfort of the patient and facilitate the nursing. In the upper extremity the swivel ring modification permits of the arm being placed at the side, and makes transportation easier. In hospital it is desirable that some modification of this splint be made because of the danger to the joint function and the possibility, in severe septic conditions in the neighborhood of the elbow, of ankylosis of the elbow joint. In splinting which must be more or less prolonged, where there is danger of ankylosis, the principle should always be kept in mind that the limb should be placed in the most useful functional position should ankylosis occur. Further, at as early a period as possible function should be stimulated by permitting active, or at least passive, movements of the joints of the extremity. Needlessly prolonged splinting is still a most fruitful source of loss of function.

My colleague, Dr. George Wilson, has developed a modification of the Thomas splint for use especially in the upper arm, which has proven very efficient in our clinic. The extension is obtained by incorporating the upper end of the wire splint into a plaster of paris band about the chest, thus doing away with the ring pressure in the axilla which is always a source of discomfort and danger if long maintained.

Non-Union—That sepsis is not a large factor in the production of non-union has been amply demonstrated in the large series of war fractures. The chief causes of non-union are, first:—gaps due to loss of substance of bones, from early removal of many of the comminuted fragments, or second:—lack of apposition from interposition of muscle or fascial structures. The comminution of bone rather tends to increase the amount of callus thrown out, and increases the probability of union. The removal of these fragments makes gaps between the ends, and non-union is likely to occur. In septic conditions the inflammatory reaction increases the bone growth and with reasonable approximation union will always occur. Very few of the fragments found even in severely crushed bones are so completely separated from all soft structures as to endanger their blood supply, and most of these can be brought fairly well into line by splinting and some replacement at the time of primary cleaning up. Bone lacking approximation in septic conditions, without union, may be brought into line usually by splinting with extension, removal of the intervening tissue, and fixation by heavy kangaroo tendon inserted through a drill hole in the fragments far enough from the ends to hold securely. The extension and support with the Thomas splint usually will be effective in holding the position by the time the sutures are absorbed.

The fixation of fragments in septic fractures by steel plates or bands, so freely advocated by some surgeons, has been shown to be harmful and for the most part to destroy the prospect of early healing. Even when plates are put on as a temporary measure to act as internal splints, with the expectation of their removal at an early date, they usually defeat the object sought. The series of drill holes for insertion of screws opens up the interior of the bones to infection, and when the plates are removed it is found that a necrotic area the size of the affixed plate usually results. There may be a mass of callus all about the plate, sometimes burying it,

but the necrotic area will sequestrate and union necessarily must be delayed or in some cases, as shown by Mr. Hey Groves, the whole thickness of bone becomes necrotic, and its sequestration leads to a gap between the bone ends. The fixation is not greater than that secured by absorbable material, as fascia or kangaroo tendon, as the screws rapidly loosen and pull out, and dependence must be placed on the splinting for continued fixation.

The non-union which may have resulted from failure to remove fibrous tissue separating the bone ends undoubtedly is best treated by an autogenous bone graft. The time at which this bone graft should be done has been a debated question, but experience has shown that approximately a year should elapse after all sinuses have healed before grafting should be attempted. Even after this period foci of infection have been uncovered. When the infection is gross enough to be certain the operation should be delayed, for while in certain cases bone grafts remain and union is accomplished, in more cases the graft is extruded and the operation fails. In non-union due to gaps in the case of single bones, as the humerus or the femur, the bone ends should be approximated and the graft inserted, even if a considerable degree of shortening results. In bridging gaps in one of the bones of the forearm or leg it is never good judgment to shorten the remaining solid bone to permit approximation of the ends of the other. These gaps may be bridged by an autogenous graft even when the distance is four inches or more. The success of such graft depends largely on the close approximation of the graft to the bone into which it is planted. We have found that the diamond shaped graft fitted into a long straight cut, in the case of small bones like the ulna or radius, is most efficient. By springing the edges of the straight cut the wedge graft can be so tightly placed as to hold without other fixation. In large bones like the tibia the V cut is made slightly narrower than the diamond shaped graft and the latter is driven firmly into place. A period of perfect splinting with plaster of paris or other efficient material should be maintained for three months at least before union may be looked for. Failures are usually due to sepsis, poor approximation or imperfect splinting.

After perfect healing and solid union of these fractures has taken place the function of the limb may be very imperfect. The muscles controlling the joints above or below the fracture may be tremendously tied up with scar tissue or the muscle may be in part destroyed or removed. The movements of the neighboring joints thereby are very much restricted. A prolonged course of hydrotherapy and massage should be employed to hasten the recovery of function and put the patient back into his place as a wage-earner. Neglect to follow up cases after union is secured, to see that adequate after treatment is carried out, is responsible in large measure for the long periods of disability from which these patients suffer.

PRESENT DAY EVOLUTION OF MAN

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Is man still in process of Evolution? As a species, biologically considered, is he progressive, stationary or retrogressive? Is there evidence that man has changed biologically in historic times, that contemporary man is undergoing hereditary change, or that continued change may be anticipated in future prospect?

To the Western mind the idea of progress is everywhere so evident that it would seem idle to question its biological application to present day man, but a closer analysis of the nature of human progress reveals a common confusion in thought on two processes which are really distinct—progress in civilization vs. biological progress.

As to progress in civilization there can of course be no doubt. Our social inheritance—the products of man's mind, to wit, language, science, art, institutions, the many inventions—accumulates and builds higher with every passing generation of man at an ever increasing pace. Like the latest runner in a relay, the younger generation starts forth from the vantage points freshly gained by its predecessor. To this relay process there would seem to be no end or limit.

With the biological inheritance it is quite otherwise. Fortunately or unfortunately each new generation begins biologically with germ cells, at practically the same point from which its parents began. Lamarckian environment-inheritance and use-inheritance are negligible factors. The acquisitions of the parents are biologically practically wholly lost to the new generation, and it is open to serious question whether permanent changes in the germ cells ordinarily arise from them. Social betterment by no means necessarily implies direct and corresponding improvement of the innate characters of the race, any more than social worsening implies the contrary. "Race is deeper than culture."

Biologists agree generally that evolution as a process working itself out in the series of organisms has resulted on the whole in progress (with some retrogression), in increasing diversity of forms (with some convergences) and in adaptations (with many surviving disharmonies). Doubtless man as a species and the several races and sub-races with all their characteristics, physical and mental, were evolved in the later stages of the same process, as the numerous lines of evidence affirm. Could we safely project the curve from the past into the present and future, we would certainly expect to find evolution still continuing as something natural, necessary and inevitable, and promising to continue indefinitely towards its final limits through the operation of the causes responsible for evolution in lower forms: natural and sexual selection, isolation, hybridization, mutation, and the other factors, which also directed changes in man's past history, and which helped evolve in him his superior mentality and social solidarity. There is abundant raw material for human evolution, for man exhibits extraordinary (though definitely limited) diversity and variability in colour, features, head-

form, brain size, stature, freedom from constitutional diseases, resistance to infectious diseases, mental normality, intelligence, gifts and talents, etc.

Natural vs. Social Selection

But the evolution of human society and civilization has gradually revolutionized conditions of existence from those prevailing in the early history of the race. Man is "nature's insurgent son," a "rebel" who strives through the social inheritance to become more and more independent of his environment, to control and direct the natural processes. He aims mentally to adapt the environment (climate, food, etc.) to himself rather than himself to environment; hence physically he changes slowly and has remained unspecialized, except perhaps for his erect posture and large brain. By inventions, discoveries and mutual aid he has become able to "evade, ameliorate, or mitigate" the effects of natural selection, and somewhat to mollify or even sometimes to nullify the struggle for existence against physical conditions, against other organisms, and even that between the races. As Darwin suggested, "With highly civilized nations, continued progress depends in a sub-ordinate degree on natural selection."

Civilization is, in fact, accompanied by so many agencies opposed to natural selection that many claim it makes for biological deterioration. The downward path of degeneracy is easy to follow, as it has been followed times innumerable by other species, and possibly by some of the backward races of men. The age of invention and industrial revolution with its attendant city and indoor life, congested populations, changed food habits, over-specialization, occupational and venereal diseases, and increased use of conveniences and tools without doubt hinder individual development in many different ways and may help account for the prevalence of the characteristically modern ailments: cancer, appendicitis, diabetes, nephritis and other metabolic or endocrinal diseases, diseases of heart and arteries, and the nervous and mental diseases. But hereditary deterioration and permanent racial decadence are not to be expected as a *direct* result. The anatomical studies of mummies by Eliott Smith have demonstrated that man has remained essentially unchanged since early Egyptian days, with at most minor and uncertain decline in size of the fifth toe, of the wisdom teeth, in amount of hair on body and head, in perfection of sense organs, etc. Nor have the characters of the races then living since changed; Egyptian, Semite, and negro were as clearly differentiated then as now, and apparently had already long existed as separate races. The essential race characters are notoriously permanent despite centuries of life in unwonted climates and with changed habits. Is even this time too brief to detect movement in biological timepieces? A human generation is not more than a few seconds in the day of human evolutionary history!

Modern life does effect evolutionary change *indirectly* in some respects by its opposition to natural selections. Some see striking evidence that modern war is a detrimental agency, eliminating first the strongest and the best. Medicine and surgery, hygiene and sanitation, charity and humane sentiment tend to favour continuance and even the multiplication of undesirables "who would not be tolerated under nature's régime." In so far as defects and weaknesses are hereditary their unrestricted

reproduction is sure to result in some deterioration of the human average. The Eugenists, Galton, Pearson, Davenport and Goddard, have pointed out scores, in fact over a hundred, of human diseases and defects, physical, mental and moral, of various degrees of seriousness and undesirability—feeble-mindedness, epilepsy, choreic insanity, neuropathic constitution, pauperism, deaf-mutism, hereditary cataract, hemophilia, malformations of hands, etc., etc.—which run down persistently generation after generation in family lines, and are only too freely reproduced, and some of which appear to increase and spread through the normal population at alarming rates. Through high birth rates, an *un-natural* selection has recently operated to increase the proportion of certain hereditarily unfit and subnormal types.

A similar unfavourable reproductive selection is evident also in the relatively high birth rate of the lower levels of normal mentality. Pearson's English statistics showed that one-sixth of the marriages, mostly of the less provident and responsible classes, produce one-half of the total children. Meanwhile the birth rate of the leading classes, the highly trained, and presumably the best endowed and the most capable (?) through late marriage and restriction of births has rapidly declined toward a two-child standard, as in France, which number is so insufficient to replace the parents and make up for deaths in childhood, for failures to marry, or childless marriages, that these classes tend rather to decrease in most civilized countries. "All the big families live in the little houses, and the little families in the big houses." It is a "dilemma of civilization" that it tends to eliminate its best blood, that most capable of supporting high civilization and of adding to the social inheritance. Unless ability is equally distributed through all the classes, which is unlikely, civilization would seem to be a self-limiting process.

Obviously the remedies for these evils lie not in "Return to Nature" but in more civilization. The task suggests conscious social control, at least to equalize the birth rates of the different classes, to discover, perpetuate and increase the most capable and talented strains in all levels of society, and to restrain the multiplication of the most undesirable. In the alleviation of human distress and misery greater attention will surely be paid that part of the programme dealing with control of heredity. The medical ideal is all away from mere treatment of symptoms and toward detection and elimination of underlying causes. The highest and most humane preventive hygiene is race hygiene, Eugenics, working toward the ideal that none shall be born unfairly handicapped. Else "present kindness may bring future cruelty." "Until the last removable impediment in man's own nature dies childless, human reason will not rest."

But has civilization really diminished the rigour of natural selection in all respects? Despite the increasing checks on infectious and epidemic diseases and the remarkable successes in prolonging of average life an added 15 years (the maximum length of life has not increased), the question arises: Is not disease taking to-day less of those of sound and healthy constitution and more who have congenital weakness and hereditary diathesis to disease? Pearson thinks that selection is still a prominent factor in 50 to 80 per cent. of all deaths. It is possible that sanitation, quarantine and vaccination may decrease average resistance, and that old diseases may in a future generation reappear and find man,

unfortified, an easy prey. Even now, as total death rate decreases rapidly, we see a steady increase in deaths from "constitutional" and "organic" diseases (cancer, nephritis, heart disease, etc.). Certain inherited weakness shows up inevitably, finally, in spite of attempts to bolster up disharmonies. Low infant mortality in the first year of life sometimes results in a somewhat greater death rate a few years later in early childhood. Those with extreme hereditary defects and low resistance appear foredoomed, as in prehistoric times, to be weeded out by early death.

So far as death rate is concerned, intelligence and morality seem to be decided factors of advantage under modern conditions. The most intelligent are in some senses the fittest to survive. There is, for instance, a high correlation between inheritance of longevity and general health and fertility and low infant mortality; and low intelligence is associated with high infant mortality and with high accident rate in industry.

Isolation Passing

Racial divergence in early days resulted in part from inbreeding of people in geographic isolation, on islands, plateaus, in river valleys, or in mountains, separated by natural barriers. Inbreeding tends always to develop and establish more or less homogeneous locally adapted races, each differentiated from other similar tribes and peoples. Communication, travel, and migration have lately broken down the old isolation, and ushered in the era of cosmopolitanism and social democracy, and produced (1) an ever increasing competition of races in all parts of the world, and (2) extensive hybridization of contiguous races. Each of these processes is acting now more rapidly than ever before to alter the components of the human species.

Within a few centuries the white race, largely through its early advances in practical science and medicine has been able to obtain control of three-fourths or more of the land area of the earth, and in this to colonize and expand. The European Whites, especially the Nordics, have grown phenomenally from an insignificant European population to one out-numbering any other race, yellow, brown, black or red; and they have possession of much of the sparsely inhabited land in which to increase further.

Selection by Climate and Disease

Contact of the different races in a given region generally means that one at least of the races has entered new territory and climates and met with new conditions and new diseases. On account of different inherited characters and different powers of controlling environment and disease the different races meet these conditions with unequal success. The Hawaiians have within a century declined from a flourishing population of 150,000 to less than 24,000, and the loss has been replaced by Japanese and whites. The Polynesians everywhere, the native Australian, and the North American Indian were in different degrees unable to withstand the white man's diseases and habits of life. Even without wars and without intent, merely through deep-seated physiological causes, the Caucasian has exterminated many backward, nomadic, and unadaptive

races. The Maoris of New Zealand have a folk-saying, that, just as the white man's rat has exterminated the native rat, and his plants driven out many native plants, so the white man himself will surely extinguish the Maori—as the Maori did the Moriori before him. In South Africa Hottentot and Bushman are disappearing before the colonists, but the strong and intelligent Kaffirs are different—they outbreed the whites and bid fair to reverse the usual situation and dispute the possession of the Cape.

The diseases of civilization swept over Europe in repeated epidemics or steadily took their toll, eliminated the susceptible, and left the hardy and resistant; but they seldom visited the natives of other regions in their isolation. Hence the latter are extremely unresistant and are often half-exterminated at first contacts with tuberculosis, measles, small pox, influenza, as their extraordinary mortality rates still show. The death rate of negroes in the Northern States and in cities generally far exceeds their birth rate. As compared with whites they are more than twice as susceptible to tuberculosis and pneumonia, and more than seven times as prone to venereal disease with its resultant frequent mortality and sterility. In the United States as a whole the negro's "anticipation of life" is fifteen years less than the white's. Between the various white immigrant groups there, differential death rates are also for some reason revealed: the Irish are especially susceptible to diseases of the lungs, heart, and kidneys, the French-Canadian shows high mortality from tuberculosis and high percentage rejections for military service on account of defectives, the Jewish display much nervous instability but are freer from tuberculosis, varicose veins, etc., and, like the Slavs, have a very low infant mortality.

The natives, in turn, were selected for resistance to their own, *i.e.*, tropical diseases and climates, and in tropical conditions the European is often at a disadvantage despite his medical science. In Ceylon in a recent year malaria caused among the whites a death rate twenty-two times that of the negroes and three times that of the native Indian or Malay. In West Africa the blacks are similarly favoured. The negro is particularly free from skin diseases or metabolic diseases, and is relatively immune to hookworm and other internal parasites, and, like the Indian and many other natives, to cancer.

As population becomes more cosmopolitan, more intermingled and denser, and food and space and opportunity to increase are more limited, natural selection in peaceful competition by birth rates and death rates may be renewed again intensively, even though all the races are by then inspired by sentiments of mutual aid and altruism.

Inter-racial Hybridization

Crossing is inevitable wherever races are in contact. Despite race pride or prejudice, legislation or social ostracism, alliances, legitimate or illegitimate, occur repeatedly, and more or less race fusion results. South Italians are in varying degrees a complex blend of early Roman, colonial Greek, Carthaginian Semite, Saracen, Norman, and African; Cape Verde islanders of Portuguese and negro slave; East Europeans of Slav and Mediterranean and Nordic and Semitic and Asiatic. Fishbein has shown that the Jews in every old country have come to resemble the

local gentile peoples through taking in their blood, and now in West Europe the majority of Jewish marriages are interracial. One-time slavery and recent immigration have made real melting-pots of some countries, like Brazil; or like Peru, where the blood of the native Incas is thoroughly intermingled with that of Spanish Whites, Chinese, and Negroes.

Some think it only a matter of time until the then surviving men will be of one great hybrid stock. What its chief components might be would depend upon the population changes of the immediate future, when the empty spaces of the world are being filled. Possibly there will ultimately be an equatorial zone of darker people grading off to lighter toward the poles!

To the biologist hybridization is a potent factor of evolution. In plant and animal breeding hybrids between not too diverse stocks sometimes exhibit unusual vigour and always show an increased variability due to Mendelian recombination of traits, as ancestral characters are resolved and re-shuffled at each new generation. To manipulate and guide intelligently the variety and diversity of combinations unit-characters of the human races will certainly offer almost limitless possibility for good or ill.

Such responsibility in prospect will challenge the biologist, the psychologist, the sociologist, and the economist, to renewed study and co-operative effort.

SURGICAL DRESSINGS

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As with fashions in other things, fashions in surgical dressings vary from time to time, and in different localities. These variations, however, have to do with unimportant details rather than with fundamental principles; the latter having changed but little since the role played by bacterial organisms in causing suppuration first became generally recognized.

There are two types of surgical dressing in common use, the moist dressing and the dry dressing. The dry dressing is used for wounds that are expected to heal without suppuration, and is therefore the type of dressing employed after practically all "clean" operations, where, as a result of the pre-operative preparation of the part and of the aseptic technique during the operation, the region may be presumed to be reasonably free from bacteria. The chief object of the dry dressing is to protect such a wound from subsequent infection by organisms from the outside and from irritation from any other cause, such as dirt or friction. There is, however, one other point that must be considered. In no case can we be absolutely certain by any means of preparation, that the skin has been rendered completely sterile. We know, however, that the few organisms that may be left are, in the majority of cases, quite well dealt with by the defences of the tissues; but occasionally conditions are present that are so favourable to bacterial growth that even a few organisms may sur-

vive and result in suppuration and the breaking down of the wound. One of these factors, favouring the growth of bacteria, is the presence in the wound of tissue that has been devitalized by manipulation during the operation, a condition which, of course, cannot be prevented by any type of dressing. The other factor is the collection, in the region of the wound, of moisture from the skin secretions and from the blood and inflammatory exudate which are always present in greater or less amount. This moisture not only encourages bacterial growth, but also interferes with the coagulation of fibrin between the two cut surfaces, the first step in the process of healing by first intention; and therefore the dry dressing in addition to being a mere protection, should be of such a nature as to absorb moisture from the region of the wound and to permit evaporation from its surface.

In its simplest form it consists of a piece of sterilized gauze, folded so as to be of about twelve layers in thickness, in contact with the wound, covered with a pad of sterilized absorbent cotton, the whole being held in position on a limb by a roller bandage and on the trunk by adhesive strapping or a binder. Such a dressing, in the absence of any signs to indicate suppuration, is left in place until the stitches are removed, and then renewed until the scabs have dropped off the wound and stitch-holes—a sign that healing is complete. This simple dressing is usually all that is necessary for wounds produced under aseptic conditions, and is the one in routine use in most hospitals.

There are, however, cases in which the risk of organisms growing in the escaped blood is increased—cases for instance in which a plaster cast is applied and the dressing is to be left undisturbed for several weeks, or cases in which, owing to extensive dissection at the operation, much oozing is likely to occur. In such cases primary healing may be expected, and a dry dressing is therefore indicated, but in order to prevent the growth of any organisms accidentally contaminating the blood-clot, it is wise to use, instead of the plain gauze, a gauze impregnated with some antiseptic. Lister found, after experimenting with a great many antiseptics, that the double cyanide of zinc and mercury was the most satisfactory, and no improvement on this has since been found. The cyanide is insoluble, and for fear that stray organisms might escape the action of the antiseptic before it became moistened by the wound discharges, and be conveyed to the wound, Lister moistened the first layer of the cyanide gauze with carbolic acid. With our improved aseptic technique, this step is usually omitted, and now, in cases where we fear infection in the clot we use the cyanide gauze, with the addition of some non-irritating antiseptic dusting powder like bismuth formic iodide, which helps to keep the wound dry and inhibits bacterial growth in the escaped blood.

In addition to being used on clean operation wounds, the dry dressing may be used on accidental wounds that have been sutured, when the bruising of the tissues and the soiling of the cut surfaces are so slight as to make healing by first intention likely.

In some locations, such as on the face or scalp, the fixation of the dressing by a bandage or adhesive plaster is awkward or unsightly. In these cases a neat and efficient way of holding the dressing in position is by means of collodion. A piece of gauze, just large enough to cover the wound and sutures is laid in position and held there by wisps of absorbent

cotton fixed around the edge by means of collodion applied with a brush.

Whenever infection has occurred or is expected to occur, a moist dressing should be used. This applies to operation wounds that have become accidentally infected, wounds made for the drainage of abscesses, accidental wounds that cannot be thoroughly cleansed and freed from devitalized tissue, and any granulating surface. The primary idea in the moist dressing is to obtain drainage—to permit the free escape of discharges rather than their accumulation in the wound. The moist dressing promotes the flow of the discharges from the depths of the wound into the dressing by virtue of the capillary attraction of the absorbent strands of gauze moistened with the lotion. This capillary action is interfered with unless evaporation from the surface is possible, and for this reason a moist dressing applied for drainage should never be covered by anything impermeable like oiled silk. The dressing should consist of several pieces of gauze, each about twelve layers thick, folded into convenient sizes (4 in. x 4 in. and 4 in. x 8 in. suit most needs) and soaked in the lotion as warm as can be comfortably borne; the whole being covered by a pad of absorbent cotton and retained in position by a bandage or taped adhesive straps. When the provision of drainage is important, the dressing should be renewed or moistened as often as it dries, i.e., every two or three hours, but where drainage is less important, a change once or twice a day, depending on the amount of discharge, is sufficient. In addition to its action in promoting capillary drainage, the moist dressing prevents clotting of the pus about the wound and in the drainage tubes, and by virtue of its heat causes some hyperaemia, which is an aid in combatting infection. Also, as practically all the lotions used are antiseptic, there is at least some deterrent action on the growth of bacteria.

Many different lotions have been advocated for the dressing of infected wounds, and it is no uncommon thing to find each surgeon in the same hospital using a different solution. The reason for this is probably that none of them are quite satisfactory or possess any outstanding advantages. As used in the ordinary moist dressing, they cannot, by their bactericidal action, sterilize the tissues in the depths of the wound; the most that can be expected from them, as antiseptics, is that they will limit to some extent the growth of organisms in the wound and prevent infection by new strains introduced from without. Any antiseptic is of necessity a protoplasmic poison and injurious to the tissue cells. The ideal antiseptic would destroy bacteria, even in the presence of wound discharges, and, at the same time would leave the tissues unharmed. Unfortunately such an antiseptic is not available, and the nearest approach to this ideal is probably found in the group of chlorine antiseptics, of which Dakin's solution and eusol are probably the best known, but difficult to prepare and keep, but of which the proprietary chlorazene is a handy and useful example. It should be remembered, however, that the chief use of the moist dressing is to promote drainage, and that its antiseptic action is never great. The realization of this fact is probably the reason why most surgeons prefer to use as lotions solutions that are essentially non-irritating to the tissues, and do not possess great antiseptic powers, such as boracic acid, 1-40.

During the war, Carrel made a serious attempt to sterilize wounds, or at least to so reduce the number of organisms present that the wound

could be safely closed by suture. After opening up all sinuses, he introduced a number of small rubber tubes, tied at their ends, and with numerous perforations in the terminal inch or so. These tubes were so placed that they would convey the antiseptic to all surfaces, and through them be instilled, at intervals of one or two hours, a quantity of Dakin's solution (neutral sodium hypochlorite). He found that by this frequent flooding of the whole wound with a powerful antiseptic, he was able, in a week or ten days, to reduce the number of organisms found per microscopic field in a smear of the wound discharges, to one or two. This degree of cleanliness—two organisms or less per microscopic field—he called his "suture standard", and showed that wounds that had been brought to such a condition—now of course covered with granulation tissue—could be safely sutured ("secondary suture"), and in the majority of cases would heal. This is practically the only method of wound treatment where the antiseptic action of the lotion predominates. Its technique—and if it is carried out at all it should be carried out exactly as its author outlined it—is decidedly tedious, and the method is seldom used now in the ordinary hospital where infected wounds, of sufficient size to make it worth while, are rare.

A further problem in dressing is presented by the large superficial granulating wound, seen typically in extensive fourth degree burns. Here, the lesion being entirely superficial, efficient drainage is easily obtained. The chief problem is to avoid anything that will interfere with the process of healing by granulation. The ordinary moist dressing, each time it is changed, pulls off the tender granulations on the surface, causing bleeding and interfering with repair. To avoid this we combine an ointment with the moist dressing, by smearing the surface of the gauze evenly with borated vaseline before dipping it in the lotion. The addition of the ointment in this way prevents the sticking of the gauze to the granulations, and at the same time interferes very little with the drainage.

In conclusion, it might be well to emphasize the following points. The dry dressing is to be used on all wounds expected to heal by first intention, and needs to be changed only at infrequent intervals. The moist dressing should be used on all wounds where drainage is required, and should be changed frequently, depending on the amount of the discharge. The lotion used in the moist dressing should be chosen rather for its lack of harmful action on the tissues than for its bactericidal action. And finally, every dressing should be applied and changed in such a way as to avoid all injury to the tissues that will interfere with the process of repair.

THE ANATOMICAL BASIS OF VOLUNTARY MUSCLE TONE

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The word "tone" is used to express the state of slight tension in which healthy voluntary muscle is kept throughout life.

This state of tonus depends upon the integrity of a reflex arc which is presided over by the cerebellum. In disease of this organ the most outstanding physical sign is the loss of tone, or Atonia, of the voluntary

musculature and it is therefore of extreme value to understand the anatomical disposition of the nerve paths by means of which the cerebellum is able to maintain muscle tone in the normal body.

Anatomy

In order that the cerebellum may accurately control the tone of muscles and alter the intensity of this tone as required by change in physiological conditions, it is necessary that it receive afferent or sensory nerve impulses. These impulses are brought to the cerebellum by two outstandingly important routes.

From the General Sensory Surface of the body as well as from the Muscles themselves come afferent nerve impulses which enter the cerebellum through the two Spino-cerebellar Tracts.

From the Vestibule and Semicircular Canals of the Internal Ear the Cerebellum receives information via the Vestibulo-cerebellar Tract.

These three tracts carry their impulses to the cortex of the cerebellum which acts as the discriminating factor or reflex centre of the arc.

The efferent path from the cortex to the muscles consists in the first place of a Purkinje nerve cell and its axon which carries the efferent stimulus from the cerebellar cortex to one of the internal nuclei of the cerebellum—principally the Nucleus Dentatus. From this nucleus a fresh neuron leaves the cerebellum by its superior peduncle and ascends to end in the Red Nucleus of the Midbrain. There a third neuron arises, the axonal process of which becomes one of the fibres of the Rubro-spinal Tract which carries the tone-impulse to the Spinal Cord. This axon is thought to end by synapsing round a motor nerve cell in the anterior horn of grey matter of the Cord from which the impulse can be transmitted down the motor nerve to the voluntary muscle.

This, then, is the pathway of the reflex arc of muscle-tone. There are two further anatomical facts remaining to be considered.

The first of these is that each half of the cerebellum controls the musculature of the same half of the body. The afferent nerve path of the reflex arc is uncrossed, the impulses brought by the right spino-cerebellar and vestibulo-cerebellar tracts reaching the right cerebellar cortex. The efferent side of the arc shows a double decussation which amounts to the same thing, for practical purposes, as no decussation at all. The first decussation occurs between the Cerebellum and the Red Nucleus and consequently fibres from the right cerebellar hemisphere will end in the left Red Nucleus. Owing, however, to the decussation of the Rubrospinal Tract immediately after its origin, the fibres from the Left Red Nucleus will run down the Right Rubrospinal Tract and will be distributed to the musculature of the right side of the body. The right cerebellar reflex arc therefore controls the musculature of the right side of the body, and vice versa.

The second point to be dealt with is the Cerebral Control of the Cerebellum. From the frontal and temporal areas of the cortex of the Cerebrum arise the Frontopontine and Temporopontine Tracts. These end in the Pontine Nuclei and are uncrossed. From the nerve cells of the pontine nuclei arise axonal processes which cross the median line and enter the opposite hemisphere of the Cerebellum by the Middle Cerebellar Peduncle. These axons end in the Cerebellar Cortex. Hence the Cere-

bral Cortex sends nerve impulses to the Cerebellar Cortex of the opposite side of the body.

Lastly, it must not be forgotten that by means of the Corticorubral Tract the Cerebral Cortex is able to exert an influence on the Rubrospinal Tract directly and independently of the cerebellum.

Cortical Localization in the Cerebellum

A great deal of research work is being done with the object of allocating to different areas of the cerebellar cortex the function of the control of tone for different groups of muscles. Bolk, for instance, has come to the conclusion by experimental removal of portions of the cerebellum in animals, that in the middle lobe of the organ can be found cortical centres which maintain the tone of head, eye, neck and trunk musculature and for that of certain synergic movements of the limbs. In the anterior part of the lateral lobe of the cerebellum he finds the centres for the muscles of the upper limb and in the posterior part of the lateral lobe centres for the lower limb musculature.

This localization of areas for different muscle groups is however still very much "sub judice" on account of the differing and often contradictory results of different observers. Gordon Holmes in his Croonian Lectures in 1922 speaking from his wide clinical experience of cerebellar lesions, said: "My observations consequently lend no support to a circumscribed or focal representation of different portions of the body in the cortex of the cerebellum, apart from the fact that the vermis is concerned mainly with movements requiring the co-operation of muscles of the two sides of the body, and the lateral lobes mainly with the functions of the homolateral limbs."

Clinical Tests for Lack of Muscle Tone

The clinical tests for impairment of muscle tone are very numerous and it is only proposed to deal briefly with two of these which illustrate the principles involved.

(a) Fixation Nystagmus.

When a normal person is asked to look at a point placed at one of the extreme lateral limits of his field of vision he is able, by contracting the external rectus of one eye and the internal rectus of the other, to keep his eyes steadily fixed on that point. If, however, the external eye muscles are lacking in normal tone, the patient is unable to keep them firmly contracted and they consequently tend to roll away from the object looked at. To counteract this rolling away movement the patient has voluntarily to contract the appropriate external and internal recti to bring the eyes back to the object required to be viewed. Hence there is produced a jerky, oscillating movement of the eyeballs known as Nystagmus, which consists of a frequently repeated series of two movements, the passive rolling away of the eyes followed by the voluntary "jerk back" of the eyes into their position for viewing the object. This nystagmoid movement of the eyes is more marked when the patient is asked to look to the same side as that of his cerebellar lesion.

(b) The "Pendulum" Knee-jerk.

If a normal person's knee-jerk is tested in such a position that the leg can swing freely, one contraction of the quadriceps takes place and the

leg immediately comes to rest in the vertical position. This is due to the action of the hamstring muscles which, by their tonic tension, prevent the leg swinging backwards and forwards before it finally comes to rest.

If the hamstrings are deficient in their tonic contractile power, as is the case in a patient with a lesion of the same side of his cerebellum, the leg swings passively backwards and forwards after the knee-jerk extensor contraction has taken place until it finally takes up its vertical position of rest.

THE DISCOVERY AND PREPARATION OF INSULIN

F. G. Banting and C. H. Best.

There have been numerous reviews of the literature which deals with attempts to prepare potent pancreatic extracts for the treatment of experimental or clinical diabetes. The representative of this journal assures us, however, that it is advisable to refresh the memories of the students of the University of Toronto by brief references to some of the earlier work in this field.

Previous to the year 1889 several investigators had suggested a connection between the pancreas and the disease, diabetes. In that year von Mering and Minkowski proved very conclusively that the complete removal of the pancreas from dogs and other animals resulted in the production of very marked diabetes.

In the year 1869, Paul Langerhans had described those cell groups in the pancreas which are now called the Islands of Langerhans.

Lepine was the first to suggest that the pancreas furnished an internal secretion necessary for the proper metabolism of sugars and fats. Diamare, Shaffer and others have suggested that the islands are the seat of production of the internal secretion of the pancreas. D'Arnozan and Vaiélard, Sscobolew, W. G. MacCallum, and others, have shown that the ligation of the ducts of the pancreas results in the degeneration of the acinous cells which produce pancreatic juice, but that the islet cells remain undisturbed by this procedure.

Since the work of von Mering and Minkowski, hundreds of investigators have attempted to prepare from the pancreas a substance which when administered to diabetic animals would alleviate the symptoms of diabetes. Among these investigators the names of Zuelzer, Scott, Rennie, Murlin and Kramer, Kleiner, Clark, Knowlton and Starling, and Paulesco are prominent. Zuelzer and Scott worked on the hypothesis which was later independently formulated by one of us (F. G. B.). Zuelzer prepared alcoholic extracts of pancreas and administered them to dogs made glucosuric by the injection of epinephrine. He obtained encouraging results for a time but his research was later abandoned. Scott attempted to ligate the pancreatic ducts of dogs but his operations were not successful. He also unsuccessfully attempted to extract the glands with alcohol and we now know that the concentrations he used are unfavorable for the extraction of insulin. Kleiner's experiments with watery extracts of normal dogs' pancreas deserve mention. He obtained some slightly beneficial effects by the administration of these extracts to dia-

betic dogs. His results were not conclusive, however, and his work was not continued.

In 1921 authorities were agreed that all attempts to demonstrate the internal secretion of the pancreas had met with either negative or inconclusive results.

The hypothesis upon which our experiments were founded was that some constituent of the external secretion of the pancreas was antagonistic to the hypothetical internal secretion for which Professor Shaffer of the University of Edinburgh had suggested the name "Insuline". This hypothesis was presented to Professor Macleod of this University and he was able to provide advice and facilities for putting it to the test. Work was commenced in the Department of Physiology on May 16th, 1921. It was originally supposed that only some six or eight weeks would be necessary to test the hypothesis.

In order to eliminate the external secretion of the pancreas it was proposed to take advantage of the above mentioned fact that the acinous cells degenerate after the ligation of the pancreatic ducts. Our first work was therefore to ligate the pancreatic ducts of a number of normal dogs. The animals recovered quickly from the operation and none of them showed any symptoms or signs of diabetes. In the interval required to secure degeneration of the pancreas, we obtained records on totally depancreatized dogs which we contemplated using as test objects. The extreme heat of the summer of 1921 made it very difficult for us to keep the diabetic animals in reasonably good condition and we were not in a position to test any material until late in July.

On July 27th, we decided to make our first test. We anaesthetized a dog whose pancreatic ducts had been ligated some ten weeks previously and removed the degenerated pancreas. The gland was smaller than normal and very firm in consistency. It was immediately sliced into a chilled mortar containing Ringer's solution and the mixture was frozen. After several hours the frozen material was allowed to thaw slowly and the tissue was finely macerated with sand and a pestle. The liquid was then strained off and filtered through paper. This filtrate was the original pancreatic extract used in our experiments. This material was administered by intravenous injection to a diabetic dog. The material exerted a slightly favorable effect upon the blood sugar and sugar excretion of the animal. This experiment was not at all conclusive but extremely encouraging to us, and we made haste to repeat it. Subsequent experiments were very successful and we consistently observed that the administration of this extract of degenerated pancreas resulted in the marked lowering of blood sugar, the diminution of sugar excretion, and phenomenal improvement in the general condition of completely diabetic dogs. The administration of a single large dose of this material often changed a listless semi-comatose diabetic dog into a bright, active animal. Visitors to our working quarters during the months of August and September were greatly impressed with the remarkable effects of this extract. Professor C. L. Starr and Dr. George Young were among the first to witness a demonstration of the beneficial effects of the extract containing the long-sought-for internal secretion of the pancreas. The kindly interest and help of Prof. Henderson was of inestimable value at this stage.

We then proceeded to secure more information concerning the pro-

perties of the extract and its effects upon diabetic animals. It was found that sugar given with the extract was retained to a much greater extent than was the case when it was administered in the absence of the extract. Incubation of the extract with pancreatic juice resulted in the complete destruction of the active material.

When Professor Macleod returned from Europe in September he observed the effects of the administration of the extract. In view of the great importance of the fundamental observation that the active principle of the extract exerted a definite influence upon the blood sugar and sugar secretion of diabetic animals, he advised us to secure even more results along this line. We did this, and in addition were able to show, among other things, that very active extracts could be prepared from other more readily available sources. Active extracts were prepared from the pancreas of foetal calves, taken at a stage of development before the pancreatic ferments had appeared. Potent extracts from normal adult ox pancreas were also secured. To obtain this latter material we extracted finely divided ox pancreas with acidulated alcohol. We consider this a very important experiment since all large scale methods for the preparation of insulin to-day have the acid alcohol extraction as the first step in the process. It was shown that a completely diabetic dog could be kept alive and healthy for at least 10 weeks by the daily administration of this whole gland extract.

The practical application of these results was very evident and in view of this it was deemed advisable to secure the co-operation of other investigators. This was about the middle of December, 1921. Professor J. B. Collip was invited to participate in the biochemical side of the investigation, and was provided facilities by Professor Fitzgerald and Professor Defries of the Connaught Laboratory. A little later Mr. E. C. Noble, Drs. J. Hepburn and J. K. Latchford began work on Insulin under the direction of Prof. Macleod in the Department of Physiology. The work of this group in the winter of 1921-22 resulted in the demonstration of a number of very important facts. It was ascertained that the administration of insulin enabled a completely diabetic dog to store large amounts of glycogen in its liver. It will be remembered that diabetic animals are unable to store greater than 2 per cent. of glycogen in the liver in the absence of insulin even when very large quantities of sugar are administered. It was found that the respiratory quotient of diabetic dogs could be definitely raised by the administration of carbohydrate and insulin. This experiment proved conclusively that insulin caused the burning of carbohydrate in the diabetic organism. The extracts used in the first experiments in which glycogen was found in the livers of completely depancreatized dogs and in some of the respiratory quotient experiments, were prepared from adult ox pancreas by our original method. This group also recognized the deleterious effects of overdoses of insulin and discovered that sugar was a very efficient antidote. The effects of insulin upon various forms of experimental hyperglycaemia were studied, particularly by Mr. E. C. Noble. Drs. Hepburn and Latchford showed that the presence of insulin resulted in the increased consumption of sugar by the perfused mammalian heart.

The first insulin administered to diabetic patients in the Toronto General Hospital was prepared from normal ox pancreas by the original

method. This material exerted a definite effect upon the blood sugar and sugar excretion of a diabetic patient. Certain objectionable effects, however, were observed, which were undoubtedly due to the large percentage of protein which this extract contained.

Professor Collip with the knowledge of the properties of the material which we had obtained and with some additional information which he secured by very extensive work, was able in a very short time to purify the original extract so that much of the objectionable inert material was eliminated. The results of the short study of the clinical effects of this material were reported by Drs. Campbell and Fletcher of the Toronto General Hospital, in collaboration with Professor Collip and ourselves.

It will not be possible, in the space at our disposal, to review in detail the various modifications and improvements which have been introduced in the methods of preparation of insulin. A brief summary of some of the more important contributions is submitted. Insulin was originally prepared from the ox pancreas, as stated above, by the extraction of fresh glands with faintly acid alcohol. The concentration of alcohol in our original experiments varied from 40 to 60 per cent. The alcoholic solution of pancreas was filtered and the filtrate concentrated by evaporation of the alcohol and water in a warm air current. Lipoid material was removed by extracting the residue with toluene or ether. The resulting product was the original whole gland extract. We were able to show that the active material contained in this extract was practically insoluble in 95 per cent. alcohol. Professor Collip used acid alcohol as the initial extractive but raised the concentration to about 80 per cent. By this means certain inert objectionable materials were removed. The inert materials were filtered off and the insulin precipitated from the alcoholic solution by raising the concentration of alcohol to approximately 92 per cent. The precipitated material was dissolved in distilled water. Certain difficulties were encountered when it was attempted to apply this method to a larger scale production and various modifications were introduced by the workers in the Connaught Laboratories in the spring of 1922. It was found that the final product obtained by these methods was not sufficiently pure for prolonged clinical use, and efforts were made to secure a better product. The benzoic acid method of Moloney and Findlay which depends upon the fact that insulin is absorbed from watery solution by benzoic acid was successfully used in the Connaught Laboratories for several months. Professor Shaffer of Washington University, St. Louis, and his collaborators, Somogyi and Doisy, introduced a method of purification which is known as the isoelectric process. This method depends upon the fact that if a watery solution of insulin is adjusted to approximately PH 5 a precipitate settles out which contains much of the potent material and relatively few impurities. Dudley has found that insulin is precipitated from watery solutions by picric acid and he has made use of this fact to devise a very ingenious method for the purification of the active material. Mr. D. A. Scott, and one of us (C. H. B.), who are responsible for the preparation of insulin in the Insulin Division of the Connaught Laboratories, have tested all the available methods and have appropriated certain details from many of these. Several new procedures which we believe are advantageous have also been introduced. The method of preparation of insulin which may be seen in operation at any time in the Insulin Division, is as follows:—

The beef or pork pancreas is finely minced in a large grinder and the minced material is then treated with 5 c.c. of concentrated sulphuric acid, appropriately diluted, per pound of glands. The mixture is stirred for a period of three or four hours and 95 per cent. alcohol is added until the concentration of alcohol is 60 to 70 per cent. Two extractions of the glands are made. The solid material is then partially removed by centrifuging the mixture and the solution is further clarified by filtering through paper. The clear filtrate is concentrated in vacuo to about 1/20th of its original volume. Ammonium sulphate (37 gms. per 100 c.c) is then added to the concentrate and a protein material containing all the insulin floats to the top of the liquid. The solid material is skimmed off and dissolved in water. Certain inert materials are eliminated by adding alcohol to this watery solution so that the concentration of alcohol is approximately 80 per cent. An equal volume of ether is then added to the 80 per cent. alcohol and the precipitate which forms contains practically all the potency which was present in the alcoholic solution. The solution of this precipitate in water is adjusted to approximately PH 5 and a white flocculent precipitate settles out. The solution of this latter precipitate in acid water (PH 2.5) is the final product as it is distributed at the present time.

ATOMS AND IONS

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Being well aware of what the majority of medical students think in their innermost being of the subject of pure physics, one almost feels like apologizing for attempting an article on such a purely theoretical question as "atoms and ions." However, if one recalls the many phases in which electrical phenomena make their appearance in the human body in the process of life, no apologies should be necessary. The transfer of nerve impulses to and from the nerve centres, the sensitivity to change of ion concentration exhibited by the blood and other body fluids, the inter-action of membranes and colloidal solutions in the body, all point to the intimate connection between life processes and electrical action, and open up a field of investigation for years to come.

As it is undoubtedly true that the phenomena with which we have to do in electrolysis of solutions are of prime importance in all these electrical actions, the investigations of the real structure of ions should be of great interest. As a result of Davy's and Faraday's work of a hundred years ago, one is led to believe that there exists in conducting solutions of all kinds carriers of electricity and further, that each carrier is able to transport a very few definite unit quantities of electricity. These carriers, the so-called ions, are loaded with either positive or negative electricity which they give up to the electrodes when they arrive. For example, in a solution of common salt the molecules of sodium chloride seem to break up into sodium and chlorine carriers or ions, the former bearing one unit charge of positive electricity, the latter one unit charge of negative electricity; the sodium ion carries its charge to the negative electrode, delivers it there, and immediately appears in

the guise of a sodium atom. Not until the charge is delivered does the sodium ion become a sodium atom. Analogous action takes place with the chlorine ion which, on giving up its negative charge, becomes a chlorine atom. In what way do the atoms of sodium and chlorine differ from the ions of sodium and chlorine?

During the last twenty years considerable advance has been made in our knowledge of the intimate structure of atoms. Three conclusions, based on experiment, are now universally accepted by physicists:

(1) That electrons which are very small negatively charged particles of definite mass and charge form a common constituent of all kinds of matter and consequently of all atoms. (The mass of an electron is about 1/1800 of the mass of an atom of hydrogen.)

(2) That the actual number of electrons per atom is determinable for different kinds of atoms.

(3) That any atom as a whole is electrically neutral, *i.e.*, that it possesses equal quantities of positive and negative electricity.

Our picture of an atom, then, is that it is a combination of negatively charged electrons and something bearing a positive charge equal in magnitude to the total charge on the electrons present. Many theories as to the relative lay-out of the positive and negative parts have been suggested; the most widely accepted view now held is that due to Rutherford, viz., that an atom consists of a nucleus of a definite number of units of positive electricity acting as a centre of force for a planetary group of electrons, the combined negative charge of which is equal in magnitude to that of the positive charge on the nucleus. It is still an open question what the spatial relation of these electrons actually is.

Very convincing experiments on the number of electrons per atom lead to a unique coincidence; if one writes down the elements in the order of their atomic weights and numbers the list 1, 2, 3, etc., the number attached to the elements in the list happens to be the number of electrons in its atom, as shown by the partial list in the accompanying table.

	1 H						
2 Helium	3 Li	4 Be	5 B.	6 C.	7 N.	8 O.	9 Fe
10 Neon	11 Na	12 Mg	13 Al	14 Si	15 P.	16 S.	17 Cl.
18 Argon	19 K						

When minute study of this table was made it was found that the class of rare and inert gases have interesting numbers of electrons. A more complete list of these gases is the following:

Helium	2	Krypton	36 = 18 + 8 + 8 + 2
Neon	10 = 8 + 2	Xenon	54 = 18 + 18 + 8 + 8 + 2
Argon	18 = 8 + 8 + 2		

In view of the quantitative relations between the quantity of electricity carried and the amount of chemical transformation taking place during electrolysis, there must exist a very close connection between chemical affinity and electrical forces, which leads one to suspect that the electron plays a very important part in chemical action. Now the remarkable property of each of the above gases is that they form absolutely no compounds which probably accounts for the fact that they escaped detection for so long. An entire lack of ability or disposition to form compounds with other chemical elements or even among themselves,

suggests that each of these atoms forms a stable, self-contained system of positive charges and negatively charged electrons and that aptitude to form stable compounds shown by other individuals among the elements is due to an attempt to reproduce such a stable, self-contained combination.

The numbers given in the second list have been broken up into sums of simpler numbers. Helium is the first inert substance, therefore two electrons and not one or three or four represents an exceedingly stable, self-satisfied group about a nucleus. That atom which has only one electron, hydrogen, will take up another with avidity; that atom which has three, lithium, will not be very averse to losing one of its three. As we go up the list of the first table 2+8 is the number giving the next inert, self-satisfied combination; this suggests that eight electrons, arranged in some way, around the inner two, give a very stable equilibrium to the atom. Fluorine (with 9=2+7) will be very anxious to annex another electron to produce the stable combination 2+8, while sodium (with 11=2+8+1) has one electron which is superfluous to the stable combination. So going on up the list, we find that chlorine (with 17=2+8+7) would be on the look-out for another electron, while potassium has one which can be easily detached.

To return, then, to the question of common salt, sodium chloride. When the sodium atom comes within the range of action of the chlorine atom the two atoms are united so that the outer electron belonging to sodium completes the stable combination for the chlorine atom, and thus the two make a secure union.

When this molecule is brought into contact with water, a disrupting action breaks the constituents apart, but the chlorine steals away with the outer electron of the sodium, leaving the sodium as a whole positively charged (the sodium ion) and the chlorine negatively charged (the chlorine ion). Only when brought into contact with the electrodes by outside electric forces are the ions brought again to the state of atoms of sodium and chlorine.

In general, an ion is an ordinary chemical entity which has been endowed with a positive or negative charge by an unnatural loss or gain of an electron.

A CONSIDERATION OF SOME LIVER FUNCTION TESTS

Ivan R. Vaile, '24.

The liver is an organ of the greatest importance in the body economy. It supervises all the material entering the blood stream from the digestive tract and regulates the amounts of the various substances necessary for the maintenance of well-being. Too great quantities are not permitted to enter the circulation at once. Thus, for instance, sugar is held back in the liver and stored as glycogen. Fats if taken in liberal amounts, are kept back in the liver until such time as there is a demand for this substance. Proteins, likewise, are partly retained and partly worked up into amino-acids and urea. The liver also has the faculty of detoxicating a great many poisonous substances. Another function of the liver is to work up the material contained in the effete red blood cells into a substance necessary for the service of the body.

Phenoltetrachlorphthalein Test—Abel & Rowntree[12], by means of pharmacologic studies, determined that phenoltetrachlorphthalein is excreted almost entirely by the liver, and that when injected intravenously it is not toxic. Rowntree, Hurwitz and Bloomfield[13], and Whipple, Mason and Peightal[14] used phenoltetrachlorphthalein as a test for liver function by determining the amount excreted in the stools during the 48 hours subsequent to its injection intravenously. Further studies with this method were carried out by McLister & Frazier[15], Kahn & Johnston[16], Chesney, Marshall & Rowntree[17], and Krumbhaar[18]. Their reports are conflicting and this method has not met with extensive clinical usage. Legitimate criticisms of this method are that it is not only time consuming and disagreeable, but also not reliable, in that quantitative stool collections are frequently inaccurate indices of the entire intestinal contents. Furthermore, the dye may be reabsorbed from the large intestine and re-excreted by the liver.

In 1916, McNeill[19] introduced the method for testing liver function by determining the time required for the dye to appear in the bile, obtained through the duodenal tube. The fallacy of this method was soon evident and methods were introduced by Aaron, Beck & Schneider[20] and Piersol & Bockus[21] for the quantitative estimation of the dye in the bile obtained through a duodenal tube. This method at best is uncomfortable to the patient, time consuming, and there is a considerable percentage error due to the escape of varying amounts of bile around the duodenal tube, which passes down the intestine and makes quantitative values uncertain.

In an attempt to avoid the drawbacks of the duodenal method, Rosenthal[22] devised a method based on the ability of the liver to remove the dye from the blood stream. He studied this method experimentally[23] and showed that after intravenous injection of a given dose per body weight, the dye normally leaves the plasma very rapidly and with remarkable uniformity. Striking degrees of retention of this dye in the blood appear to exist when liver damage was produced experimentally by chloroform and phosphorus poisoning. When the dye was injected during the stage of jaundice and toxaemia, large amounts remained in the blood over a prolonged period. After convalescence was established curves of disappearance approaching normal were obtained. In the early jaundice due to mechanical obstruction, before there had resulted any extensive damage to the liver cells, it was shown that the dye could be removed from the blood stream in practically normal time, except that a trace remains in the plasma for 24 hours or longer.

Technique—

(1) Weigh the patient.

(2) With a needle of moderate bore, shaken free from water, a superficial vein of the arm is entered, and about 8 c.c. of blood is allowed to run into a clean, dry, test tube. Through the same needle inject the dye.

(3) Inject 5 mg. per kilogram (2.2 lbs.) of body weight intravenously under asceptic precautions . Dissolve the phthalein in 30 c.c. saline and wash in the dye with another 25-30 c.c. of saline. Inject slowly.

(4) With a small needle--(a large hypodermic size may be used)—and syringe which has been washed in physiological saline, from 2-4 c.c. of blood is withdrawn from a vein of the opposite arm, 15 minutes after

the injection of the dye, and again at 1 hour. Later samples may be taken if indicated by the findings in the hour sample. Care must be taken not to use salt solution or needles that have been in contact with the dye, as it is easily decolorized.

(5) The drawn bloods are allowed to clot in the test tubes and then centrifuged. The plasma is pipetted off into separate small test tubes of uniform size and one drop of 5 per cent. Na OH for every c.c. is added to each tube in order to bring out the maximum colour.

(6) *Preparation of a Standard*—10 mg. of the dye is added to 100 c.c. of water. This strength has been arbitrarily chosen as a standard for comparison, as it represents the approximate concentration that would be reached if all the injected dye remained in the plasma. With the sample of plasma obtained before the injection of the dye, which should be clear, a series of standards is prepared in small test tubes of the same size. The plasma in which the amount of dye is to be determined is now matched with these standards using naked eye comparison in a good light. Artificial light is not satisfactory.

Preparation of Standard—

2 c.c. 100 per cent. *S.S.	2 c.c. 80 per cent. *S.S.	2 c.c. 60 per cent. *S.S.	2 c.c. 40 per cent. *S.S.	2 c.c. 20 per cent. *S.S.	2 c.c. 12 per cent. *S.S.
.6 c.c. Plasma	.6 c.c. Plasma	.6 c.c. Plasma	.6 c.c. Plasma	.6 c.c. Plasma	.6 c.c. Plasma
25 per cent.	20 per cent.	15 per cent.	10 per cent.	5 per cent.	3 per cent.

*S.S. = Standard Solution.

With the dosage given, the dye is normally removed from the blood stream very rapidly. In normal human beings from 2 to 6 per cent. is present in the plasma 15 minutes after injection and practically complete disappearance takes place within from 40 to 60 minutes. In cases of liver disease high percentages may be found in the plasma for many hours after injection.

Rosenfield & Schneiders[24] have recently used this test in normal pregnancy and the toxaemias of pregnancy. In normal pregnancy they have found the liver to be uninvolved as determined by the test. The toxaemias of pregnancy, including eclampsia show a definite relation between the degree of liver impairment, as measured by this test, and the degree of toxicity, as evidenced by the clinical picture. Toxaemias of pregnancy, including eclampsia, show definite liver impairment, and subsequent to relief from toxic symptoms there is a return of liver function to normal limits. Greenbaum and Brown[25] have studied the liver function with the phthalein test in cases of acute and chronic syphilis under treatment and in various skin diseases. Arsenic, and therefore the arsenobenzenes, have a strong affinity for liver cells and a mild grade of hepatitis may be produced during syphilitic treatment without any clinical symptoms. They observed that the test was but slightly or not at all altered in patients who received from 1 to 45 intravenous injections of the arsenobenzenes. 75 per cent. of the patients who had received from 45 to 124 intravenous injec-

tions of arsphenamine or neo-arsphenamine, or both, showed no liver dysfunction. Patients who develop a toxic icterus are apt to suffer later from permanent liver dysfunction. When the acute phenomena have disappeared the permanent liver damage is not associated with apparent clinical disturbances. The test should be performed on all those syphilitic patients showing some form of intolerance to arsenic (itching, tingling in the extremities and mild dermatitis, particularly). Icterus is too late a sign of toxicity.

Van den Bergh Reactions—The first important paper on this subject was published in 1913 by Van den Bergh and Snapper, but later the whole of the available material was collected by Van den Bergh in a monograph —"Der Gallenfarbstoff im Blute"—published in 1918.

The view held by Van den Bergh is that the polygonal cells of the liver are not essentially concerned with the manufacture of bile pigment, but have chiefly to do with its transference from the vascular capillaries into the bile capillaries. It seems probable that in passing through the polygonal cells, bilirubin is modified in some way, and that this is the explanation offered at present to account for the two varieties of bilirubin made evident by the Van den Bergh reaction. The view is also put forward that it is the reticulo endothelial cells, either in the spleen or liver (Kupffer cells) which deal with the breaking down of haemoglobin and the elaboration of bile pigment. This view is based entirely on animal experiments in which during blood destruction, bile pigment, haemosiderin and fragmented red cells have been seen together in the endothelial cells of the liver. No one has ever seen bile pigment in the polygonal cells of the liver in healthy human or animal livers.

The site of origin of bilirubin has been a matter which has received considerable investigation and the views held up to the present time are largely influenced by the experiments of Whipple & Hooper.[26] They performed two series of experiments: (1) the injection of haemoglobin into dogs with the liver, spleen and intestines shut off from the rest of the circulation; and (2) the injection of haemoglobin into dogs with a head and thorax circulation only. They found that in both types of experiment, haemoglobin was rapidly changed, in part at least, into bile pigment within the circulating blood. McNee[28] repeated the experiments using a much more sensitive test for bilirubin than available to Whipple & Hooper at the time—the Van den Bergh reaction—has been unable to confirm his results. A re-investigation of the work of Whipple & Hooper by Rich[29], has shown that the experiments which have led to the conclusion that circulating haemoglobin can be rapidly transformed into bilirubin outside the liver are not valid because the method employed—that of observing changes in animals with the so-called head and thorax circulation supposedly independent of the rest of the viscera need not actually exclude the liver from the circulation. The presence of unsuspected collateral circulation must always be reckoned with. In his investigation the liver was not merely tied off from all obvious vascular connections but was actually extirpated and the fate of introduced haemoglobin studied. Transformation into bilirubin was never observed under such conditions.

Icterus essentially depends on an increase of pigment in the serum. Thorlich discovered that if a small amount of a diazonium salt in acid solution be added to an alcoholic solution of bilirubin, coupling occurred

with the formation of an azo-dye—azo-bilirubin. Thereafter the method appears to have been forgotten until revived by Van der Bergh. Biliverdin and other yellow substances which may rarely be present in human serum and which at first sight imitate bilirubin, do not give the reaction. Van der Bergh observed that in some cases it was unnecessary to bring the bilirubin into alcoholic solution, and that a positive coupling with the production of an azo-dye can be obtained by adding the diazo-reagent direct to the icteric serum.

Icteric sera may be divided therefore into 3 groups:

(1) Sera giving a colour reaction at once (maximal within 30 seconds) on the addition of the diazo-reagent directly to the serum. This is known as the *immediate or direct reaction.*

(2) Sera giving no color reaction, or only after a long delay, on the addition of the diazo-reagent direct to the serum. This is known as the *delayed direct reaction.*

(3) Every icteric serum gives an immediate colour reaction with the diazo-reagent, after precipitation with alcohol so as to bring the bile into alcoholic solution.

An immediate or direct reaction indicates obstruction. A biphasic reaction may be obtained—a slight prompt coloration occurs at once, followed after a variable delay by gradual deepening of the colour reaction. It can best be accounted for on the view that both the variety which gives the prompt reaction and that which gives the delayed reaction, are present in the serum together. It can again be divided into biphasic prompt and biphasic delayed according as one or other variety predominates.

Technique of the Test—

(1) Obtain a small amount of blood in a clear, dry test tube and allow to clot. Remove the serum with a pipette.

(2) Freshly prepared diazo-reagent. This consists of two solutions each of which keeps well, but the mixture must only be made prior to the test.

Solution A—

Sulphonilic Acid, 1 gram.
Concentrated HCl., 15 c.c.
Distilled water, 1000 c.c.

Solution B—

Sod. nitrate, 0.5 gm.
Distilled water, 100 c.c.

The diazo-reagent consists of a mixture of A and B in the proportion of 25 c.c. of A to 0.75 c.c. of B.

(3) To 1 c.c. of the serum (may be diluted with 2 c.c. or more of distilled water) 0.25 or 0.5 c.c. of the freshly prepared diazo-reagent is added.

One of three things may occur:

(a) Immediate reaction—bluish violet colour in 10-30 seconds. This is characteristic of jaundice due to complete obstruction.

(b) Delayed direct—begins after 1-15 minutes or even longer and consists in the development of a reddish colour which gradually deepens and becomes more violet. This type of reaction is particularly characteristic of haemolytic jaundice. The actual amount of bilirubin present is determined by the indirect method.

(c) Biphasic reaction—a reddish colour appears at once which either slowly or quite rapidly deepens to violet.

(4) The indirect reaction. To 0.5 c.c. of the serum add 1 c.c. of 96 per cent. alcohol. Centrifuge until all the albuminous material has sunk to the bottom. To 1 c.c. of the supernatant fluid add 25 c.c. of diazo-reagent. In the presence of bilirubin a violet-red color appears and is maximal almost at once. Compare with a colorimeter; the Autenrieth-Funk pattern is suitable.

It is important to have the test tubes and pipettes scrupulously clean.

The chief clinical application of this test is to differentiate between obstructive and haemolytic jaundice or functional derangement of the cells. The information furnished by this test in acute cases is reliable, but in chronic cases of obstruction there may be a change from the direct reaction to the indirect or delayed reaction.

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Editor's Note:—The conclusion of the consideration of the liver function tests and a summary will be found in the March issue of the Journal.

CASE NOTES OF HIPPOCRATES

The first medical treatise to give form and spirit to the practice of medicine was written by Hippocrates, a native of the island of Cos, in the fifth century before Christ. Medical observers all down through the centuries since his age have praised the truly great nature of his work. Of him Moynihan says: "If the power of wide and accurate generalization be, as I believe it to be, among the supreme accomplishments of the human mind, then Hippocrates may in truth be said to have had few rivals, if indeed he has had any, among all those who in later times, and in all countries, have devoted themselves to the science of medicine." We are, however, too apt sometimes to consider Hippocrates as simply one of the shadowy names of history and forget

the fact that his observations even when considered with the fuller knowledge of to-day are startling in their accuracy and insight. It gives us no little shock to find that this Greek physician gives directions concerning the arrangements of the operating room, the placing of the patient, the care to be taken of the surgeon's hands which indicate a skilled practitioner.

An instance may be quoted not only to show the fact that disease does not change but to illustrate the very accurate observations which Hippocrates made and the essentially sound principles upon which he based his clinical methods. He notes with the accuracy of a modern case-report what we now term "Cheyne-Stokes" respiration. This peculiar type of breathing was described by John Cheyne and William Stokes of the Dublin school of medicine about 1812 and bears their name. Here is the ancient memorandum in which a case probably showing Cheyne-Stokes breathing is recorded:

"Philiscus," Hippocrates writes, "who dwelt near the wall of the city was laid up. On the first day fever acute; he perspired; night very disturbed. Second day, aggravation of symptoms; night quiet. On the morning of the third day, and up to noon, appeared full of pain; but in the evening acute fever, with perspiration, thirst and dry tongue; night disturbed; he did not sleep at all; his mind wandered on all subjects. On the fourth day, general paroxysms; night more endurable. On the fifth day about noon a little blood escaped from the nostrils; night distressing and little sleep; talkativeness; delirium; extremities very cold, and could not be warmed; he rested a little towards day-break; lost speech; had a cold sweat; extremities livid. About the middle of the sixth day he died. The respiration was throughout *large and rare like that of a person who required to be reminded to breathe.*" Galen, commenting upon this passage, attached the meaning, "like a person who forgot for a time the need of breathing, and then suddenly remembered."

With this contrast the words of Dr. Cheyne in 1816. "For several days," he wrote, in his account of an elderly patient, "his breathing was irregular; it would cease for a quarter of a minute, then it would become perceptible, though very low, then by degrees it became heavy and quick, and then it would gradually cease again. This revolution in the state of his breathing occupied about a minute, during which there were about thirty acts of respiration."

These two memoranda make an interesting study—the one of modern origin, the other from the hand of the great master of medicine.

NOTES AND COMMENTS

Open Meeting

The first open meeting of the year was held on Jan. 16 in the Anatomical Lecture Room. The speaker of the evening was Dr. T. C. Routley, secretary of the Ontario Medical Association. He gave an intensely interesting address on the subject of Medical Ethics. His discourse was pleasantly interspersed with many amusing anecdotes of life as a medical undergraduate about the year

1915. At that time Dr. Routley was President of the University of Toronto Medical Society. Mr. E. H. Doney, of the First Year, rendered a solo, which was heartily encored. The Medical Orchestra was on hand to enliven any lull in the programme.

Theatre Party

About 300 medical students attended the Theatre Party at the Royal Alexandra on Monday evening, Jan. 21st. The audience was exclusively medical. Doctors, nurses and students filled the theatre to almost overflowing and followed with interest Sir John Martin Harvey's portrayal of "Oedipus Rex", a Greek tragedy. The eminent actor, supported by a strong caste, made an otherwise unappealing play very interesting.

Cloak Room

The question of the stealing of hats and coats from the T. G. H. and Pathology Building has at last, apparently, been satisfactorily settled. The University authorities early in the year consented to establish a checking system. This is now installed in the students' room in the T. G. H. It is to be hoped that all students will take advantage of this opportunity and thus the possibility of this thieving continuing will be minimized.

Representatives to Sister Institutions

Mr. R. J. Heffering represented the Toronto Medical Society at a dinner given by the Queen Aesculapian Society at Kingston, Jan 24, 1924. Mr. K. C. McCarthy of 2T5, was our representative to the Arts Ball; Mr. R. C. Montgomery, 2T4, represented at the Dental At-Home.

Medical Bureau

Undergraduates and graduates are reminded that the Ontario Medical Society have arranged a bureau whereby doctors may get in touch with young graduates or students regarding appointments. Anyone wishing further information may obtain same from Dr. T. C. Routley, Secretary, Ontario Medical Association, 180 College Street, Toronto.

Elections

Undergraduates are reminded that the annual nominations for the Medical Society Executive for 1924-25 will be received Friday, Feb. 15. Speech night will be Feb. 18, and election will be held on Feb. 22.

Medical Song

The Medical Society are desirous of obtaining a song that will be suitable as a Faculty song. Kindly forward contributions to Room 107, Anatomy Building.

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Minister of Health and Labour for Ontario